CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-341s000

REMS

APPENDIX A: REMS

NDA 22-341 VICTOZA (liraglutide [rDNA origin] injection)

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

- To inform providers about the risk of acute pancreatitis (including necrotizing pancreatitis) and the potential risk of medullary thyroid carcinoma associated with Victoza®.

- To inform patients about the serious risks associated with Victoza®.

II. REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each VICTOZA prescription. VICTOZA is dispensed in cartons containing either two or three pre-filled disposable pens with cartridges that can deliver doses of 0.6 mg, 1.2 mg, or 1.8 mg. A copy of the Medication Guide will be packaged in each carton. Therefore, Novo Nordisk will meet the requirements of 21 CFR 208.24 for distribution and dispensing of the Medication Guide.

Additional copies of the Medication Guide will be available via the product website (www.victoza.com), by request through the Sponsor's toll-free information number (1-877-484-2869), and through the sponsor's sales representatives and Medical Science Liaisons (MSLs).

Please see the appended Medication Guide.

B. Communication Plan

In accordance with FDCA 505-1(e)(3), Novo Nordisk will implement the following elements of a communication plan to healthcare providers (HCP) likely to prescribe VICTOZA:

i. A Dear HCP (DHCP) Letter addressing the potential risk of medullary thyroid tumors and the risk of acute pancreatitis and appropriate patient selection will be mailed to HCP. The timing of the mailing will be within 60 days after product approval. The DHCP Letter will contain the FDA-approved labeling. The intended audience for this DHCP letter will be healthcare professionals who are likely to prescribe VICTOZA and all endocrinology specialists and others identified through professional organizations (e.g. AMA, AACE). These include physicians, nurse practitioners, and physicians' assistants, predominantly in the specialties of Endocrinology, Internal Medicine, and Family Practice. Any newly identified (through 3 years after product approval) prescribers of Victoza will be fully detailed on the contents of the Communication Plan.

Please see the appended Dear Healthcare Professional Letter.

ii. A Direct Mail Letter containing the information included in the DHCP letter will also be mailed once per year post launch for a total of 3 years to all prescribers who are likely to prescribe VICTOZA.

Please see the appended Direct Mail Letter.

iii. The Highlighted Information for Prescribers will be distributed by Novo Nordisk representatives during the first discussion of VICTOZA with all HCPs visited during the first six months after product launch. The Highlighted Information for Prescribers will also be sent with the Direct Mail Letter.

Please see the appended Highlighted Information for Prescribers.

Novo Nordisk will make the REMS, the DHCP letter, the Medication Guide, the Highlighted Information for Prescribers, and professional labeling available via a REMS-specific linkage from the VICTOZA website. The Medication Guide, the Highlighted Information for Prescribers and professional labeling will also be available via hardcopy from Novo Nordisk representatives and through Novo Nordisk's Call Center.

Please see the appended Victoza REMS landing page screenshot.

C. Elements to Assure Safe Use

The REMS for VICTOZA can be approved without Elements to Assure Safe Use.

D. Implementation System

Because the REMS for VICTOZA can be approved without Elements to Assure Safe Use, an implementation system is not required.

E. Timetable for Submission of Assessments

Novo Nordisk will submit REMS Assessments to FDA at 1 year, 2 years, 3 years, and 7 years from the date of the approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Novo Nordisk will submit each assessment so that it will be received by the FDA on or before the due date.

APPENDIX B: DEAR HEALTHCARE PROFESSIONAL LETTER

IMPORTANT DRUG WARNING

Dear Healthcare Professional:

The purpose of this letter is to inform you of important safety information about Victoza. The Food and Drug Administration (FDA) has approved VICTOZA (liraglutide [rDNA origin] injection), a once daily human GLP-1 receptor agonist for the treatment of type 2 diabetes mellitus. VICTOZA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of VICTOZA outweigh the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis. Novo Nordisk has established an informational program for healthcare professionals to help minimize these risks.

There is a Boxed Warning for VICTOZA:

WARNING: RISK OF THYROID C-CELL TUMORS

Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors.

Potential Risk of Medullary Thyroid Carcinoma

- Patients with thyroid nodules noted on physical examination or neck imaging obtained for other reasons should be referred to an endocrinologist for further evaluation.
- Although routine monitoring of serum calcitonin is of uncertain value in patients treated with VICTOZA, if serum calcitonin is measured and found to be elevated, the patient should be referred to an endocrinologist for further evaluation.

Risk of Acute Pancreatitis

- In clinical trials studying VICTOZA, there were more cases of pancreatitis with VICTOZA than with comparators.
- After initiation of VICTOZA, and after dose increases, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back, and which may or may not be accompanied by vomiting).
- If pancreatitis is suspected, VICTOZA and other potentially suspect drugs should be discontinued promptly, confirmatory tests should be performed and appropriate management should be initiated.
- If pancreatitis is confirmed, VICTOZA should not be restarted.
- Use with caution in patients with a history of pancreatitis.

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